

## Refine Search

### Search Results -

| Term   | Documents |
|--|-----------|
| (5 NOT 6).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.    | 42        |
| (L5 NOT L6 ).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD. | 42        |

**Database:**

- US Pre-Grant Publication Full-Text Database
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- IBM Technical Disclosure Bulletins

**Search:**

Refine Search

### Search History

**DATE:** Thursday, November 30, 2006    [Purge Queries](#)    [Printable Copy](#)    [Create Case](#)

| <u>Set Name</u>   | <u>Query</u>                                     | <u>Hit Count</u> | <u>Set Name</u> |
|---|--|------------------|-----------------|
| side by side  |  |                  | result set      |
| <u>DB</u> =PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; <u>THES</u> =ASSIGNEE; <u>PLUR</u> =YES; |  |                  |                 |
| <u>OP</u> =AND  |  |                  |                 |
| <u>L9</u>   | L5 not L6  | 42               | <u>L9</u>       |
| <u>L8</u>   | L6 not L7  | 55               | <u>L8</u>       |
| <u>L7</u>   | L6 and (Sendai adj virus)                        | 4                | <u>L7</u>       |
| <u>L6</u>   | L5 and (diabetic or diabetes)                    | 59               | <u>L6</u>       |
| <u>L5</u>   | L4 same (ischemic or ischemia or angiogenesis)   | 101              | <u>L5</u>       |
| <u>L4</u>   | (HGF) same (vector or DNA or (nucleic adj acid)) | 804              | <u>L4</u>       |
| <u>L3</u>   | L2 and (diabetic or diabetes)                    | 12               | <u>L3</u>       |
| <u>L2</u>   | L1 and (HGF)                                     | 35               | <u>L2</u>       |
| <u>L1</u>   | Morishita-Ryuichi.in.                            | 100              | <u>L1</u>       |

END OF SEARCH HISTORY

 **PALM INTRANET**Day : Thursday  
Date: 11/30/2006

Time: 13:14:26

## Inventor Name Search

Enter the first few letters of the Inventor's Last Name.  
Additionally, enter the first few letters of the Inventor's First name.

| <b>Last Name</b>                       | <b>First Name</b>                    |                                       |
|--|--------------------------------------|---------------------------------------|
| <input type="text" value="Morishita"/> | <input type="text" value="Ryuichi"/> | <input type="button" value="Search"/> |

To go back use Back button on your browser toolbar.

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 **PALM INTRANET**Day : Thursday  
Date: 11/30/2006

Time: 13:14:26

## Inventor Name Search

Enter the first few letters of the Inventor's Last Name.

Additionally, enter the first few letters of the Inventor's First name.

**Last Name****First Name**

To go back use Back button on your browser toolbar.

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## Welcome to DialogClassic Web(tm)

Dialog level 05.13.02D  
Last logoff: 30nov06 11:18:34  
Logon file001 30nov06 14:09:28  
>>>PROFILE is in a suspended state.  
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\* \* \*

File 1:ERIC 1966-2006/Oct  
(c) format only 2006 Dialog  
**\*File 1: ERIC, File 1, will reload soon.**  
Accession numbers will change.

Set Items Description  
--- -----

Cost is in DialUnits  
?

B 155, 5, 73  
30nov06 14:09:38 User259876 Session D953.1  
\$0.42 0.120 DialUnits File1  
\$0.42 Estimated cost File1  
\$0.03 INTERNET  
\$0.45 Estimated cost this search  
\$0.45 Estimated total session cost 0.120 DialUnits

SYSTEM:OS - DIALOG OneSearch  
File 155: MEDLINE(R) 1950-2006/Nov 28  
(c) format only 2006 Dialog  
**\*File 155: The file has resumed updating with UD20061120,**  
with RT=IN DATA REVIEW and RT=IN PROCESS records.  
File 5: Biosis Previews(R) 1969-2006/Nov W3  
(c) 2006 The Thomson Corporation  
File 73: EMBASE 1974-2006/Nov 30  
(c) 2006 Elsevier B.V.

Set Items Description  
--- -----

?

S (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME)  
12962 HGF  
320536 VECTOR  
2712891 DNA  
795495 VIRAL  
46761 LIPOSOME  
S1 1815 (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME)  
?

S S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  
1815 S1  
334106 ISCHEMIC  
396758 ISCHEMIA  
95397 ANGIOGENESIS  
S2 171 S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  
?

S S2 AND (DIABETIC OR DIABETES)  
171 S2  
327898 DIABETIC

663873 DIABETES  
S3 5 S2 AND (DIABETIC OR DIABETES)

?

RD

S4 2 RD (unique items)

?

T S4/3,K/ALL

4/3,K/1 (Item 1 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

14983812 PMID: 15253387

**Recombinant hepatocyte growth factor accelerates cutaneous wound healing in a diabetic mouse model.**

Yoshida Saho; Matsumoto Kunio; Tomioka Daisaku; Bessho Kazuhiko; Itami Satoshi; Yoshikawa Kunihiko; Nakamura Toshikazu

Division of Molecular Regenerative Medicine, Course of Advanced Medicine, Osaka University Graduate School of Medicine, Yamadaoka 2-2-B7, Suita 565-0871, Osaka, Japan.

Growth factors (Chur, Switzerland) (England) Jun 2004, 22 (2) p111-9  
ISSN 0897-7194--Print Journal Code: 9000468

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

**Recombinant hepatocyte growth factor accelerates cutaneous wound healing in a diabetic mouse model.**

We examined effects of recombinant hepatocyte growth factor ( HGF ) on cutaneous wound healing, using a full-thickness cutaneous excision model in diabetic mice. Topical administration of HGF , as well as basic fibroblast growth factor (bFGF), promoted the rate of wound closure and re-epithelialization. Both HGF and bFGF enhanced expansion of the granulation tissue and stimulated neovascularization on day 7 postwounding, wherein the increase in microvessel density in HGF -treated wounds was higher than that in bFGF-treated wounds. Matrix metalloproteinases (MMP-2 and MMP-9) activities involved in cell migration, angiogenesis , and extracellular matrix (ECM) remodeling, were enhanced by HGF -treatment on day 7. On day 28 postwounding (later stages of wound healing), granulation tissue in bFGF-treated wounds remained to a greater extent than that seen in saline- and HGF -treated wounds. Likewise, bFGF- but not HGF -treatment stimulated DNA synthesis of fibroblasts in granulation tissue, suggesting that HGF stimulates wound healing with lesser degree of susceptibility to cutaneous scarring. We propose that supplement of HGF may be a potential therapeutic approach for treatment of cutaneous ulcer.

Descriptors: \*Diabetes Mellitus, Experimental--metabolism--ME;  
\*Hepatocyte Growth Factor--metabolism--ME; \*Recombinant Proteins--chemistry  
--CH

4/3,K/2 (Item 2 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

13453880 PMID: 11696476

**Therapeutic angiogenesis induced by human hepatocyte growth factor gene**

in rat diabetic hind limb ischemia model: molecular mechanisms of delayed angiogenesis in diabetes.

Taniyama Y; Morishita R; Hiraoka K; Aoki M; Nakagami H; Yamasaki K; Matsumoto K; Nakamura T; Kaneda Y; Ogihara T

Department of Geriatric Medicine, Division of Gene Therapy Science, Biomedical Research Center, Osaka University Medical School, Suita, Japan.

Circulation (United States) Nov 6 2001, 104 (19) p2344-50, ISSN 1524-4539--Electronic Journal Code: 0147763

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... might be due to downregulation of MMP-1 and ets-1 through a decrease in HGF by high D-glucose.

?

Set Items Description

S1 1815 (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME)

S2 171 S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)

S3 5 S2 AND (DIABETIC OR DIABETES)

S4 2 RD (unique items)

?

S S1 AND (DIABETIC OR DIABETES)

1815 S1

327898 DIABETIC

663873 DIABETES

S5 25 S1 AND (DIABETIC OR DIABETES)

?

RD

S6 12 RD (unique items)

?

S S6 NOT PY>1999

12 S6

11227291 PY>1999

S7 1 S6 NOT PY>1999

?

T S7/3,K/ALL

7/3,K/1 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier B.V. All rts. reserv.

06547988 EMBASE No: 1996209871

**Effect of glucagon and hepatocyte growth factor on liver regeneration - Experimental study in hepatectomized rats in vivo**

Saeki T.; Fujita T.

Department of Surgery, Jikei University School of Medicine, Tokyo Japan  
Tokyo Jikeikai Medical Journal ( TOKYO JIKEIKAI MED. J. ) (Japan) 1996,  
111/2 (189-197)

CODEN: TJIDA ISSN: 0375-9172

DOCUMENT TYPE: Journal; Article

LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH

...liver regeneration has not been well investigated. Although the biological effect of hepatocyte growth factor ( HGF ), which is a specific hepatotrophic factor, has been widely studied in vitro, there are only few in vivo. Liver DNA content was measured as a marker indicating the ability of liver regeneration 48 hours after 70% hepatectomy in Wistar rats. Mean DNA content was significantly higher in the rats which were given a total of 0.4...

...per kg of glucagon after hepatectomy than in those without glucagon administration. Similar differences in DNA content between the two groups were found also in streptozotocin (STZ) induced diabetic rats. Stimulatory effect of HGF (4 mug per kg) that was administered into the portal vein after hepatectomy on liver...

MEDICAL DESCRIPTORS:

\*liver failure--prevention--pc; \*liver failure--surgery--su; \*liver regeneration; \*streptozocin diabetes

?

| Set | Items | Description                                    |
|-----|-------|--|
| S1  | 1815  | (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME) |
| S2  | 171   | S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  |
| S3  | 5     | S2 AND (DIABETIC OR DIABETES)                  |
| S4  | 2     | RD (unique items)                              |
| S5  | 25    | S1 AND (DIABETIC OR DIABETES)                  |
| S6  | 12    | RD (unique items)                              |
| S7  | 1     | S6 NOT PY>1999                                 |

?

T S6/3,K/ALL

6/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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21922704 PMID: 17000240

**Characterization of differential gene expression profiles in diabetic embryopathy using DNA microarray analysis.**

Reece E Albert; Ji Ilwoon; Wu Ying-King; Zhao Zhiyong  
Department of Obstetrics and Gynecology, The Arkansas Center for Birth defects Research and Prevention, University of Arkansas for Medical Sciences, Little Rock, AR, USA.

American journal of obstetrics and gynecology (United States) Oct 2006, 195 (4) p1075-80, ISSN 1097-6868--Electronic Journal Code: 0370476  
Contract/Grant No.: 20 RR-16460; RR; NCRR

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

**Characterization of differential gene expression profiles in diabetic embryopathy using DNA microarray analysis.**

OBJECTIVE: The molecular mechanisms by which maternal diabetes impairs embryogenesis are not established. This study aimed to determine the developmental genes and molecular pathways that are involved in diabetic embryopathy, by comparing gene expression profiles in the yolk sacs between the embryos of diabetic and control rats by using DNA microarray analysis. STUDY DESIGN: Diabetes was induced in female rats by injecting streptozotocin (65 mg/kg) intravenously. Glucose levels were...

... gestational day 12, embryos were explanted, and yolk sacs were collected. Total RNA, free of DNA contamination, was extracted from the yolk sacs. Complementary DNA probes were synthesized, labeled with Cy3 and Cy5 fluorescent dyes, and used to hybridize rat...

... A total of 101 genes were found to be differentially expressed between the embryos of diabetic and control rats. Analyses that used PathwayAssist (Ariadne Genomics, Rockville, MD) revealed a number of...

... and stress response (insulin 2, insulin-binding protein 1, GST pi1), cell growth (GAP43, CSF1R, HGF), calcium signaling (calbindin 3, CBP A6), and PKC signaling (PKCBP beta15, FABP5), in concert with...

... CONCLUSION: These observations show significant alterations in expression of developmental and stress response genes in diabetic embryopathy, and demonstrate, for the first time, that the yolk sac cells express insulin during...

Descriptors: \*Diabetes Mellitus, Experimental--metabolism--ME; \*Fetal Diseases--metabolism--ME; \*Gene Expression Profiling; \*Oligonucleotide Array Sequence Analysis...

6/3,K/2 (Item 2 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

20994570 PMID: 16371434

**Advanced glycation end products inhibit tubulogenesis and migration of kidney epithelial cells in an ezrin-dependent manner.**

Gallicchio Marisa A; McRobert E Anne; Tikoo Anjali; Cooper Mark E; Bach Leon A

Monash University, Department of Medicine, Alfred Hospital, Commercial Road, Prahran, Victoria 3004, Australia.

Journal of the American Society of Nephrology - JASN (United States) Feb 2006, 17 (2) p414-21, ISSN 1046-6673--Print Journal Code: 9013836

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Nonenzymatic glycation of proteins to form advanced glycation end products (AGE) is implicated in diabetic complications, including nephropathy. It was shown recently that AGE bind to the ERM (ezrin, radixin ...

... BSA on ezrin-dependent LLC-PK1 kidney epithelial cellular functions: migration and hepatocyte growth factor ( HGF )-induced tubulogenesis. LLC-PK1 cells were stably transfected with cDNA for ezrin sense, ezrin antisense...

... with ezrin antisense and dominant negative N-ezrin decreased basal tubulogenesis and migration relative to vector -only transfection, establishing the ezrin dependency of these processes. AGE-BSA (20 or 40 microM) significantly decreased HGF -induced tubulogenesis and basal migration in two vector control lines relative to BSA-treated cells. However, AGE-BSA inhibition of both HGF -induced tubulogenesis and migration was overcome by overexpressing ezrin. These results demonstrate that the AGE...

... cellular function. These changes may be relevant to detrimental renal consequences as a result of diabetes .

6/3,K/3 (Item 3 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

15347746 PMID: 15734864

**Nonviral gene transfer of human hepatocyte growth factor improves streptozotocin-induced diabetic neuropathy in rats.**

Kato Naoki; Nemoto Koichi; Nakanishi Kuniaki; Morishita Ryuichi; Kaneda Yasufumi; Uenoyama Maki; Ikeda Tomosumi; Fujikawa Kyosuke

Department of Orthopaedic Surgery, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, Japan 359-8513. grd1505@gr.ndmc.ac.jp

Diabetes (United States) Mar 2005, 54 (3) p846-54, ISSN 0012-1797--  
Print Journal Code: 0372763

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

**Nonviral gene transfer of human hepatocyte growth factor improves streptozotocin-induced diabetic neuropathy in rats.**

Peripheral neuropathy is common and ultimately accounts for significant morbidity in diabetes . Recently, several neurotrophic factors have been used to prevent progression of diabetic neuropathy. In this study, we gave repeated intramuscular injections of the human hepatocyte growth factor ( HGF ) gene percutaneously, using liposomes containing the hemagglutinating virus of Japan (HVJ), to examine therapeutic efficacy of nonviral gene transfer of HGF for experimental diabetic sensorimotor neuropathy in rats. Experimental diabetes induced by intraperitoneal injection of streptozotocin resulted in a marked tactile allodynia (but not in...

...weeks after the induction. All these changes were significantly reversed by repeated gene transfer of HGF . Furthermore, we analyzed the density of endoneurial capillaries and morphometrical changes of the nerve. The density of endoneurial capillaries, disclosing marked reduction in diabetic rats, was also reversed significantly by repeated gene transfer of HGF ; however, no considerable differences were observed morphometrically in either myelinated or unmyelinated axons. These results suggest that nonviral HVJ liposome -mediated gene transfer of human HGF has potential for the safe effective treatment of diabetic sensorimotor neuropathy.

Descriptors: \*Diabetic Neuropathies--therapy--TH; \*Gene Therapy --methods--MT; \*Gene Transfer Techniques; \*Hepatocyte Growth Factor --genetics--GE; Animals; Diabetic Neuropathies--pathology--PA; Diabetic Neuropathies--physiopathology--PP; Gene Expression--physiology--PH; Genetic Vectors; Hepatocyte Growth Factor--biosynthesis--BI; Humans...

6/3,K/4 (Item 4 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

15107597 PMID: 15466268

**Intravenous administration of hepatocyte growth factor gene ameliorates**

**diabetic nephropathy in mice.**

Dai Chunsun; Yang Junwei; Bastacky Sheldon; Xia Jinglin; Li Yingjian; Liu Youhua

Department of Pathology, University of Pittsburgh School of Medicine, 200 Lothrop Street, PA 15261, USA.

Journal of the American Society of Nephrology - JASN (United States)  
Oct 2004, 15 (10) p2637-47, ISSN 1046-6673--Print Journal Code:  
9013836

Contract/Grant No.: DK54922; DK; NIDDK; DK61408; DK; NIDDK; DK64005; DK; NIDDK

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

**Intravenous administration of hepatocyte growth factor gene ameliorates diabetic nephropathy in mice.**

Diabetic nephropathy is characterized by progressive loss of renal function, persistent proteinuria, and relentless accumulation of...

...This study investigated the potential effects of long-term expression of exogenous hepatocyte growth factor ( HGF ) on normal and diabetic kidneys. Intravenous injection of human HGF gene via naked plasmid vector resulted in abundant HGF protein specifically localized in renal glomeruli, despite an extremely low level of transgene mRNA in the kidney. In uninephrectomized mice made diabetic with streptozotocin, delivery of exogenous HGF gene ameliorated the progression of diabetic nephropathy.

HGF attenuated urine albumin and total protein excretion in diabetic mice. Exogenous HGF also mitigated glomerular mesangial expansion, reduced fibronectin and type I collagen deposition, and prevented interstitial myofibroblast activation. In addition, HGF prevented kidney cells from apoptotic death in the glomeruli and tubulointerstitium. Moreover, expression of HGF inhibited renal expression of TGF-beta1 and reduced urine level of TGF-beta1 protein. Therefore, despite the effects of HGF on diabetic nephropathy being controversial, these observations suggest that supplementation of HGF is beneficial in ameliorating diabetic renal insufficiency in mice.

Descriptors: \*Diabetic Nephropathies--therapy--TH; \*Gene Therapy --methods--MT; \*Glomerular Mesangium--pathology--PA; \*Hepatocyte Growth Factor--administration...

; Analysis of Variance; Animals; Blood Glucose; Blotting, Western; Comparative Study; Diabetic Nephropathies--physiopathology--PP; Disease Models, Animal; Enzyme-Linked Immunosorbent Assay; Glomerular Mesangium --drug effects--DE...

6/3,K/5 (Item 5 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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14983812 PMID: 15253387

**Recombinant hepatocyte growth factor accelerates cutaneous wound healing in a diabetic mouse model.**

Yoshida Saho; Matsumoto Kunio; Tomioka Daisaku; Bessho Kazuhiko; Itami Satoshi; Yoshikawa Kunihiko; Nakamura Toshikazu

Division of Molecular Regenerative Medicine, Course of Advanced Medicine, Osaka University Graduate School of Medicine, Yamadaoka 2-2-B7, Suita 565-0871, Osaka, Japan.

Growth factors (Chur, Switzerland) (England) Jun 2004, 22 (2) p111-9

ISSN 0897-7194--Print Journal Code: 9000468  
Publishing Model Print.  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: MEDLINE; Completed

**Recombinant hepatocyte growth factor accelerates cutaneous wound healing in a diabetic mouse model.**

We examined effects of recombinant hepatocyte growth factor ( HGF ) on cutaneous wound healing, using a full-thickness cutaneous excision model in diabetic mice. Topical administration of HGF , as well as basic fibroblast growth factor (bFGF), promoted the rate of wound closure and re-epithelialization. Both HGF and bFGF enhanced expansion of the granulation tissue and stimulated neovascularization on day 7 postwounding, wherein the increase in microvessel density in HGF -treated wounds was higher than that in bFGF-treated wounds. Matrix metalloproteinases (MMP-2 and...

... 9) activities involved in cell migration, angiogenesis, and extracellular matrix (ECM) remodeling, were enhanced by HGF -treatment on day 7. On day 28 postwounding (later stages of wound healing), granulation tissue in bFGF-treated wounds remained to a greater extent than that seen in saline- and HGF -treated wounds. Likewise, bFGF- but not HGF -treatment stimulated DNA synthesis of fibroblasts in granulation tissue, suggesting that HGF stimulates wound healing with lesser degree of susceptibility to cutaneous scarring. We propose that supplement of HGF may be a potential therapeutic approach for treatment of cutaneous ulcer.

Descriptors: \*Diabetes Mellitus, Experimental--metabolism--ME; \*Hepatocyte Growth Factor--metabolism--ME; \*Recombinant Proteins--chemistry --CH

6/3,K/6 (Item 6 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)  
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14659384 PMID: 14749526

**Adenoviral mediated hepatocyte growth factor gene attenuates hyperglycemia and beta cell destruction in overt diabetic mice.**  
Park Mi-Kyung; Kim Duk-Kyu; Lee Hye-Jeong  
Departments of Pharmacology, Dong-A University College of Medicine, Busan, Korea.  
Experimental & molecular medicine (Korea (South)) Dec 31 2003, 35 (6)  
p494-500, ISSN 1226-3613--Print Journal Code: 9607880  
Publishing Model Print  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: MEDLINE; Completed

**Adenoviral mediated hepatocyte growth factor gene attenuates hyperglycemia and beta cell destruction in overt diabetic mice.**  
Hepatocyte growth factor ( HGF ) is a potent mitogen and promoter of proliferation of insulin producing beta cells of pancreatic islets. To study the role of HGF , an adenoviral vector carrying the human HGF (Ad.hHGF) gene was transfected into the streptozotocin-induced diabetic mice and evaluated the effect on the blood glucose metabolism and the insulin-secreting beta...

... hHGF gene transfection resulted in amelioration of hyperglycemia and prolongation of survival period in the diabetic mice. Concomitantly adenoviral- mediated hHGF gene therapy slightly increased serum insulin concentration and the expression...

... islet. Although the proliferation of beta-cell mass was not noticeable, the beneficial effect of HGF is significant to an almost deteriorated pancreatic islets. Taken together, these data suggest that the Ad.hHGF gene therapy into diabetic mice may prevent the further destruction and present as a beneficial remedy for type 1 diabetic patients.

Descriptors: \*Adenoviridae--genetics--GE; \* Diabetes Mellitus, Experimental--metabolism--ME; \* Diabetes Mellitus, Experimental--therapy--TH; \*Gene Therapy; \*Hepatocyte Growth Factor--metabolism--ME; \*Hyperglycemia--therapy--TH; \*Islets...  
; Adenoviridae--physiology--PH; Animals; Blood Glucose--analysis--AN; Body Weight; Diabetes Mellitus, Experimental--blood--BL; Diabetes Mellitus, Experimental--genetics--GE; Hepatocyte Growth Factor--genetics--GE; Humans; Hyperglycemia--blood--BL; Hyperglycemia--complications...

6/3,K/7 (Item 7 from file: 155)  
DIALOG(R) File 155: MEDLINE(R)  
(c) format only 2006 Dialog. All rts. reserv.

14119506 PMID: 12403787

**Adenovirus-mediated hepatocyte growth factor expression in mouse islets improves pancreatic islet transplant performance and reduces beta cell death.**

Garcia-Ocana Adolfo; Takane Karen K; Reddy Vasumathi T; Lopez-Talavera Juan-Carlos; Vasavada Rupangi C; Stewart Andrew F

Division of Endocrinology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15213, USA.

Journal of biological chemistry (United States) Jan 3 2003, 278 (1) p343-51, ISSN 0021-9258--Print Journal Code: 2985121R

Contract/Grant No.: DK 47168; DK; NIDDK; DK 55023; DK; NIDDK

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Hepatocyte growth factor ( HGF ) increases beta cell proliferation and function in rat insulin promoter (RIP)-targeted transgenic mice. RIP- HGF mouse islets also function superiorly to normal islets in a transplant setting. Here, we aimed to determine whether viral gene transfer of the HGF gene into mouse islets ex vivo could enhance the performance of normal islets in a streptozotocin- diabetic severe combined immunodeficient mouse marginal islet mass model in which 300 uninfected or adenovirus (Adv...

... 05) increased in AdvHGF-transduced islets containing grafts. This anti-beta cell death action of HGF was independently confirmed in RIP- HGF mice and in INS-1 cells, both treated with streptozotocin. Activation of the phosphatidylinositol 3...

...Akt intracellular-signaling pathway appeared to be involved in this beta cell protective effect of HGF in vitro. In summary, adenoviral delivery of HGF to murine islets ex vivo improves islet transplant survival and blood glucose control in a subcapsular renal graft model in immuno-incompetent diabetic mice.

metabolism--ME; Adenoviridae--genetics--GE; Androstadienes--metabolism--ME; Animals; Cell Survival--physiology--PH; Cells, Cultured; Diabetes Mellitus, Experimental; Enzyme Inhibitors--metabolism--ME; Gene Transfer Techniques; Glucose--metabolism--ME; Hepatocyte Growth Factor...

6/3, K/8 (Item 8 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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13453880 PMID: 11696476

**Therapeutic angiogenesis induced by human hepatocyte growth factor gene in rat diabetic hind limb ischemia model: molecular mechanisms of delayed angiogenesis in diabetes.**

Taniyama Y; Morishita R; Hiraoka K; Aoki M; Nakagami H; Yamasaki K; Matsumoto K; Nakamura T; Kaneda Y; Ogihara T

Department of Geriatric Medicine, Division of Gene Therapy Science, Biomedical Research Center, Osaka University Medical School, Suita, Japan.

Circulation (United States) Nov 6 2001, 104 (19) p2344-50, ISSN 1524-4539--Electronic Journal Code: 0147763

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

**Therapeutic angiogenesis induced by human hepatocyte growth factor gene in rat diabetic hind limb ischemia model: molecular mechanisms of delayed angiogenesis in diabetes .**

**BACKGROUND:** Because no study has documented the angiogenic properties of hepatocyte growth factor ( HGF ) in a diabetes model, we examined the feasibility of gene therapy using HGF to treat peripheral arterial disease in diabetes . **METHODS AND RESULTS:** Because intramuscular injection of luciferase plasmid by the hemagglutinating virus of Japan (HVJ)-liposome method had much higher efficiency than injection of naked plasmid, we used the HVJ- liposome method to transfect the human HGF gene into the rat diabetic hindlimb model. As expected, transfection of human HGF vector resulted in a significant increase in blood flow as assessed by laser Doppler imaging and capillary density, even in the diabetes model, accompanied by the detection of human HGF protein. Interestingly, the degree of natural recovery of blood flow was significantly greater in nondiabetic rats than in diabetic rats. Thus, in an in vitro culture system, we further studied the molecular mechanisms of how diabetes delayed angiogenesis. Importantly, high-D-glucose treatment of endothelial cells resulted in a significant decrease...

... in human aortic endothelial cells. Similarly, high D-glucose significantly decreased mRNA and protein of HGF in endothelial cells. Downregulation of MMP-1 and ets-1 by high D-glucose might be due to a significant decrease in HGF, because HGF stimulated MMP-1 production and activated ets-1. **CONCLUSIONS:** Overall, intramuscular injection of human HGF plasmid induced therapeutic angiogenesis in a rat diabetic ischemic hindlimb model as a potential therapy for peripheral arterial disease. The delay of angiogenesis in diabetes might be due to downregulation of MMP-1 and ets-1 through a decrease in HGF by high D-glucose.

**Descriptors:** \*Diabetes Mellitus, Experimental--complications--CO; \*Gene Therapy; \*Hepatocyte Growth Factor--administration and dosage--AD; \*Hindlimb--drug...

; Animals; Blood Glucose; Diabetes Mellitus, Experimental--chemically induced--CI; Diabetes Mellitus, Experimental--physiopathology--PP;

Disease Models, Animal; Endothelium, Vascular--cytology--CY; Endothelium, Vascular--drug effects...

6/3,K/9 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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**Gene therapy to treat diabetic neuropathy: Improvement of diabetic peripheral neuropathy by human HGF gene transfer**

AUTHOR: Koike Hiromi (Reprint); Ishida Akihiko; Tomita Naruya  
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JOURNAL: Circulation 110 (17, Suppl. S): p126 OCT 26 2004 2004  
CONFERENCE/MEETING: 77th Scientific Meeting of the  
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20041107  
SPONSOR: Amer Heart Assoc  
ISSN: 0009-7322  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

**Gene therapy to treat diabetic neuropathy: Improvement of diabetic peripheral neuropathy by human HGF gene transfer**

ABSTRACT: Although diabetes mellitus (DM) is characterized by the premature development of microvascular and macrovascular disease, peripheral neuropathy is common and ultimately accounts for significant morbidity among patients with diabetes. The ultimate consequence of such sensory deficit involving the lower extremities may be foot ulceration...

...often leads to lower extremity amputation, a complication that is about 15 times higher in diabetic vs. non-diabetic patients. Preliminary clinical studies have demonstrated improvement in signs and symptoms of sensory neuropathy in patients with lower extremity vascular occlusive disease following intramuscular injection of naked DNA encoding vascular endothelial growth factor (VEGF). In this study, we also examined the feasibility of gene therapy using human hepatocyte growth factor (HGF) to treat peripheral neuropathy in rat diabetes model. Rat diabetes model was induced by a single intraperitoneal injection of streptozotocin (STZ) (40mg/kg). Twelve weeks after treatment of STZ, naked plasmid DNA of human HGF gene was intramuscularly injected into each the femoral biceps muscle. At 2 weeks after transfection of human HGF gene, the decrease in motor nerve conduction velocity (MCV) was attenuated. At 4 weeks after transfection, transfection of human HGF gene resulted in a significant improvement in MCV as compared to control (Non-DM control: 55.2m/sec DM control: 48.7m/sec, HGF : 55.3m/sec, P<0.01). We also examined nerve blood flow by Laser Doppler...  
...LDPI) at 4 weeks after transfection. Perfusion was significantly reduced in the sciatic nerve of diabetic rats as compared to non-diabetic rats (Non-DM control: 100%, DM control: 41%, HGF : 82%, P<0.01). In contrast, a decrease in the perfusion in diabetic rats transfected with human HGF gene was attenuated. Overall, the present study demonstrated that transfection of human HGF gene improved the neuropathy in rat diabetic peripheral neuropathy model. These data may give the important clinical application to treat diabetic neuropathy using human HGF gene transfer.

DESCRIPTORS:

DISEASES: diabetes mellitus...  
... diabetic neuropathy  
MESH TERMS: Diabetes Mellitus (MeSH...  
... Diabetic Nephropathies (MeSH)

6/3, K/10 (Item 2 from file: 5)  
DIALOG(R) File 5:Biosis Previews(R)  
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0014713488 BIOSIS NO.: 200400094245

**Prevention of diabetes using adenoviral mediated hepatocyte growth factor gene transfer in mice.**

AUTHOR: Lee Hye-Jeong; Kim Hyun-Jeong; Roh Mee-Sook; Lee Jae-Ik; Lee Sung-Won; Jung Dong-Sik; Kim Duk-Kyu; Park Mi-kyoung (Reprint)

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MEDIUM: print

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RECORD TYPE: Abstract

LANGUAGE: English

**Prevention of diabetes using adenoviral mediated hepatocyte growth factor gene transfer in mice.**

ABSTRACT: Type 1 diabetes is an organ-specific autoimmune disease caused by the cytotoxic T cells-mediated destruction of the insulin-producing beta cells in the Langerhans pancreatic islets. Hepatocyte growth factor (HGF) is a potent mitogen and a promoter of proliferation of insulin producing beta cells of pancreatic islets. To study the role of HGF via viral vector in the development of streptozotocin (STZ)-induced diabetes in mice, we have developed an adenoviral vector genetically engineered to carry the gene for human HGF (hHGF) and evaluate the change of blood glucose, insulin level, and insulin-secreting beta cells  
...

...islets. We demonstrate that the treatment with hHGF gene prevented the development of STZ-induced diabetes and increased serum insulin level to above normal range. Furthermore, it preserved pancreatic beta cells from destruction. These in vivo results may support previous findings that HGF is insulinotropic agent for beta cells and HGF treatment renders the cells to be resistant to the development of diabetes from STZ administration. We suggest that an adenoviral mediated hHGF gene therapy is a good candidate for the prevention and treatment of type 1 diabetes.

DESCRIPTORS:

DISEASES: diabetes --...

...type 1 diabetes --

MESH TERMS: Diabetes Mellitus (MeSH...  
... Diabetes Mellitus, Insulin-Dependent (MeSH)

6/3,K/11 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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11906793 EMBASE No: 2003016518

**Adenovirus-mediated hepatocyte growth factor expression in mouse islets improves pancreatic islet transplant performance and reduces beta cell death**

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Journal of Biological Chemistry ( J. BIOL. CHEM. ) (United States) 03 JAN 2003, 278/1 (343-351)

CODEN: JBCHA ISSN: 0021-9258

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 42

Hepatocyte growth factor ( HGF ) increases beta cell proliferation and function in rat insulin promoter (RIP)-targeted transgenic mice. RIP- HGF mouse islets also function superiorly to normal islets in a transplant setting. Here, we aimed to determine whether viral gene transfer of the HGF gene into mouse islets ex vivo could enhance the performance of normal islets in a streptozotocin- diabetic severe combined immunodeficient mouse marginal islet mass model in which 300 uninfected or adenovirus (Adv...

...05) decreased, and the total insulin content was significantly (p < 0.05) increased in Adv- HGF -transduced islets containing grafts. This anti-beta cell death action of HGF was independently confirmed in RIP-HGF mice and in INS-1 cells, both treated with streptozotocin. Activation of the phosphatidylinositol 3...

...Akt intracellular-signaling pathway appeared to be involved in this beta cell protective effect of HGF in vitro. In summary, adenoviral delivery of HGF to murine islets ex vivo improves islet transplant survival and blood glucose control in a subcapsular renal graft model in immuno-incompetent diabetic mice.

MEDICAL DESCRIPTORS:

...death; gene transfer; SCID mouse; adenovirus vector; hyperglycemia; glucose blood level; drug effect; protein expression; diabetes mellitus; signal transduction; nonhuman; mouse; animal experiment; animal model; controlled study; animal tissue; animal cell...

6/3,K/12 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE  
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06547988 EMBASE No: 1996209871

**Effect of glucagon and hepatocyte growth factor on liver regeneration - Experimental study in hepatectomized rats in vivo**

Saeki T.; Fujita T.

Department of Surgery, Jikei University School of Medicine, Tokyo Japan  
Tokyo Jikeikai Medical Journal ( TOKYO JIKEIKAI MED. J. ) (Japan) 1996, 111/2 (189-197)

CODEN: TJIDA ISSN: 0375-9172

DOCUMENT TYPE: Journal; Article

\* LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH

...liver regeneration has not been well investigated. Although the biological effect of hepatocyte growth factor ( HGF ), which is a specific hepatotrophic factor, has been widely studied in vitro, there are only few in vivo. Liver DNA content was measured as a marker indicating the ability of liver regeneration 48 hours after 70% hepatectomy in Wistar rats. Mean DNA content was significantly higher in the rats which were given a total of 0.4...

...per kg of glucagon after hepatectomy than in those without glucagon administration. Similar differences in DNA content between the two groups were found also in streptozotocin (STZ) induced diabetic rats.

Stimulatory effect of HGF (4 mug per kg) that was administered into the portal vein after hepatectomy on liver...

MEDICAL DESCRIPTORS:

\*liver failure--prevention--pc; \*liver failure--surgery--su; \*liver regeneration; \*streptozocin diabetes  
?

| Set | Items | Description                                    |
|-----|-------|--|
| S1  | 1815  | (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME) |
| S2  | 171   | S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  |
| S3  | 5     | S2 AND (DIABETIC OR DIABETES)                  |
| S4  | 2     | RD (unique items)                              |
| S5  | 25    | S1 AND (DIABETIC OR DIABETES)                  |
| S6  | 12    | RD (unique items)                              |
| S7  | 1     | S6 NOT PY>1999                                 |

S (HGF) (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  
12962 HGF  
334106 ISCHEMIC  
396758 ISCHEMIA  
95397 ANGIOGENESIS  
S8 1153 (HGF) (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)

?

S S8 AND (DIABETIC OR DIABETES)  
1153 S8  
327898 DIABETIC  
663873 DIABETES  
S9 41 S8 AND (DIABETIC OR DIABETES)

?

RD  
S10 21 RD (unique items)

?

S S10 NOT PY>1999  
21 S10  
11227291 PY>1999  
S11 0 S10 NOT PY>1999

?

| Set | Items | Description                                    |
|-----|-------|--|
| S1  | 1815  | (HGF) (S) (VECTOR OR DNA OR VIRAL OR LIPOSOME) |
| S2  | 171   | S1 (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)  |

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S3      5  S2 AND (DIABETIC OR DIABETES)
S4      2  RD  (unique items)
S5      25 S1 AND (DIABETIC OR DIABETES)
S6      12 RD  (unique items)
S7      1  S6 NOT PY>1999
S8      1153 (HGF) (S) (ISCHEMIC OR ISCHEMIA OR ANGIOGENESIS)
S9      41  S8 AND (DIABETIC OR DIABETES)
S10     21  RD  (unique items)
S11     0  S10 NOT PY>1999
?
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## COST

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$2.20    10 Type(s) in Format 3
$2.20    10 Types
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$7.00    1.167 DialUnits File5
$4.40    2 Type(s) in Format 3
$4.40    2 Types
$11.40 Estimated cost File5
$9.73    0.869 DialUnits File73
$9.30    3 Type(s) in Format 3
$9.30    3 Types
$19.03 Estimated cost File73
OneSearch, 3 files, 3.207 DialUnits FileOS
$1.86  INTERNET
$38.47 Estimated cost this search
$38.92 Estimated total session cost 3.327 DialUnits
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